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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,932	09/24/2004	Jeffrey P. Demuth	04132	9878

20879 7590 01/12/2007

EMCH, SCHAFFER, SCHAUB & PORCELLO CO
P O BOX 916
ONE SEAGATE SUITE 1980
TOLEDO, OH 43697

EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
31 DAYS	01/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,932	DEMUTH ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-80 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-80 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claims 1-4, 6, 7, 10-17, 19, 20, 23-30, 32, 33, 36-43, 45, 46, 49-52 (in part), drawn to methods for determining whether an agent can reduce proliferation or cause death of a cancer cell or inhibit cancer growth by determining the level of a polynucleotide marker selected from the group of one of the 13 polynucleotides set forth in Tables 1 and 5 and identifying an agent that can decrease cell proliferation when the marker is present.

Group II, claims 1, 5, 8-14, 18, 21-27, 31, 34-40, 44, and 47-52 (in part), drawn to methods for determining whether an agent can reduce proliferation or cause death of a cancer cell or inhibit cancer growth by determining the level of a protein marker selected from the group of one of the 13 proteins encoded by a polynucleotide set forth in Tables 1 and 5 and identifying an agent that can decrease cell proliferation when the protein marker is present.

Group III, claims 53 and 54, drawn to a method for diagnosing nonsmall cell lung cancer by determining the level of c-myc, E2F-1 and p21.

Group IV, claim 55, drawn to a general method for monitoring treatment by determining a gene expression profile.

Group V, claim 56 (in part), drawn to a method for treating a patient with nonsmall cell lung cancer wherein the method comprises administering to a patient an agent that modifies the expression of one of the 13 genes set forth in Table 1 and 5 or which modifies the expression of c-myc, E2F-1 or p21.

Group VI, claim 57 (in part), drawn to a method for screening for an agent that modulates the expression of one of the 13 genes set forth in Table 1 and 5 or which modifies the expression of c-myc, E2F-1 or p21.

Group VII, claims 58-66 and 78-80 (in part), drawn to a hybridization template and kits containing said template, wherein the template comprises a polynucleotides selected from the 13 polynucleotides set forth in Table 1 and 5 and c-myc, E2F-1 or p21.

Group VIII, claims 67-72 (in part), drawn to a computer system comprising the sequence information for at least 2 genes selected from the group consisting of the 13 genes set forth in Table 1 and 5, c-myc, E2F-1 and p21.

Groups IX, claims 73-77 (in part), drawn to a method of using a computer system to compare the expression level of one of the genes selected from the group consisting of the 13 genes set forth in Table 1 and 5, c-myc, E2F-1 and p21 to the level of expression of a gene in a database.

2. The inventions listed as Groups I-IX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

A 371 case is considered to have unity of invention only when there is a technical relationship among those inventions involving one or more of the same or corresponding technical features. The expression "special technical feature" means those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. In the instant application, the linking technical feature of a marker for identification of pre-malignancy does not constitute a contribution over the prior art. The technical feature linking groups I-IX is considered to be the gene of GenBank Accession No. X00351, i.e., the first nucleic acid recited in Table 1. However, this feature does not provide a contribution over the art. In particular, the NCBI database discloses GenBank Accession No. X00351, which consists of the cDNA for human beta actin. Accordingly, there is no special technical feature linking the recited groups as would be necessary to fulfill the requirement for unity of invention.

Furthermore, Groups I, II, III, IV, V, VI and IX are drawn to different methods such that each method requires different reagents and different active process steps

and the methods do not share a special technical feature. The methods of Groups I require the detection of a polynucleotide and involve identifying an agent that causes a decrease in proliferation when the polynucleotide is present in order to determine whether an agent can reduce proliferation or cause death of a cancer cell. The methods of Groups II require determining the level of a protein and identifying an agent that causes a decrease in proliferation when the protein is present in order to determine whether an agent can reduce proliferation or cause death of a cancer cell. The method of Group II requires diagnosing nonsmall cell lung cancer by analyzing the expression of c-myc, E2F-1 and p21. The method of Group IV requires monitoring treatment by administering a pharmaceutical composition to a patient and then determining a gene profile. The method of Group V requires treating a patient with nonsmall cell lung cancer with a pharmaceutical composition that alters the expression of one of the polynucleotides of Table 1 or 5 or c-myc, E2F-1 or p21. The methods of group VI requires screening for an agent that modulates the expression of one of the polynucleotides of Table 1 or 5 or c-myc, E2F-1 or p21 and requires performing the steps of StaRT-PCR and preparing a first IGEI by determining the expression level of one of the polynucleotides of Table 1 or 5 or c-myc, E2F-1 or p21 and preparing a second IGEI comprising standardized gene expression values. The methods of group IX requires the use of a computer system and involve comparing standardized numerical expression levels for one of the polynucleotides of Table 1 or 5 or c-myc, E2F-1 or p21 in a tissue or cell to the level of expression of said polynucleotides in a database. In addition to the differences in method steps, objectives, and effects, it is again noted that

the claims of the present groups are not directed to the detection or identification of molecules having the same or common special technical feature, for the reasons discussed above.

Additionally, the claimed products do not share a common property and activity, and thereby do not share a common special technical feature. The special technical feature of the polynucleotides is the identity of its monomers which are nucleotides and which determine its structure, properties and function. In contrast, the special technical feature of the proteins required for group II is the amino acid monomers of the protein, which determine the proteins structure, properties and function. The amino acids are arranged in a specific tertiary structure wherein four subunits (2 light chains and 2 heavy chains) are joined via disulfide bonds. The proteins differ from one another with respect to their amino acid sequence, secondary and tertiary structure and their functional activities. The special technical feature of the computer systems required for group VIII is the sequence information/data present in the computer system. Each set of data differs from one another with respect to its informational content. Additionally, the different products are utilized in distinct methods. While proteins can be used to generate antibodies which can then form a complex with the protein, polynucleotides and computer systems do not have these functional activities. Further, while polynucleotides may be used in hybridization assays, proteins an computer systems may not be utilized in hybridization assays. Lastly, while computer systems can be used to analyze data, polynucleotides and proteins cannot be directly used for this purpose.

Further Election Requirement Applicable to Groups I, II, V-IX

3. In addition, invention I, II, and V-IX detailed above reads on patentably distinct inventions drawn to the distinct nucleic acids and proteins selected from the group consisting of one of the nucleic acids or proteins recited in Tables 1 and 5. Further, inventions V-IX encompass the detection of one of cmyc, E2F and p21 genes, in addition to one of the nucleic acids set forth in Tables 1 and 5.

According to PCT Rule 13.2 and to the guidelines in Section (f)(i)(A) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group must have a common property or activity. Although the chemical compounds share a common structure in that they are nucleic acids and proteins, the compounds are not regarded as being of a similar nature because all of the alternatives do not share a common property or activity. Each of the polynucleotides consist of a unique nucleotide sequence and each encode a protein having a different biological activity. Similarly, each of the proteins consists of a unique amino acid sequence and has a distinct biological activity. Moreover, nucleic acids and proteins do not share a common structure and activity. The special technical feature of the nucleic acids is the identity of its monomers which are nucleotides and which determine its structure, properties and function. In contrast, the special technical feature of the proteins required for group II is the amino acid monomers of the protein, which determine the proteins structure, properties and function. The amino acids are arranged in a specific tertiary structure wherein four subunits (2 light chains and 2 heavy chains) are joined via disulfide bonds. The proteins

differ from one another with respect to their amino acid sequence, secondary and tertiary structure and their functional activities.

In response to the restriction requirement:

if Applicant elects invention I, then applicant must further elect one of the nucleic acids set forth in Tables 1 and 5 or a specific combination thereof;

if Applicant elects invention II, then applicant must further elect one of the proteins set forth in Tables 1 and 5 or a specific combination thereof;

if Applicant elects invention V, VI, VII, VIII or IX, applicant must elect one of the nucleic acids set forth in Tables 1 and 5, or one of c-myc, E2F-1 or p21 genes, or a specific combination thereof.

It is noted that this is a restriction requirement and should **not** be construed as an election of species.

4. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.
In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

5. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Carla Myers

Art Unit 1634

CARLA J. MYERS
PRIMARY EXAMINER